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Deletion of the Long Arm of Chromosome 20 in a Patient With Chronic Neutrophilic Leukemia: Cytogenetic Findings in Chronic Neutrophilic Leukemia

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We encountered a 67-year-old female with chronic neutrophilic leukemia (CNL). Cytogenetic study showed she had a deletion in the long arm of chromosome 20. This finding indicates that CNL, in this case, is a clonal disorder. Most CNL patients have normal karyotypes, and only four patients with cytogenetic abnormalities, including two cases who received chemotherapy before the cytogenetic abnormality was detected, have been reported. Four of those cases, including our case, had abnormalities in the long arm of chromosome 20. This locus may be associated with the development of CNL. To our knowledge, this is the first case with CNL who showed deletion of the long arm of chromosome 20 before treatment was started. Am. J. Hematol. 54:72–75, 1997

Key words: chronic neutrophilic leukemia; deletion; chromosome 20

INTRODUCTION

Chronic neutrophilic leukemia (CNL) is a rare disorder. The peculiar cytogenetic aberrations of CNL are unknown, since it has been reported that only a few cases with CNL show cytogenetic abnormalities. Therefore, there has been small definitive evidence of the clonal nature of CNL. We encountered a female with CNL who had clonal cytogenetic abnormality. We described the characteristics of this patient and reviewed the patients with CNL who showed cytogenetic abnormalities in this article.

CASE REPORT

A 67-year-old female visited our hospital for a chance finding of leukocytosis on September 16, 1987. She has never smoked and complained of no clinical symptoms. There was no history of neoplasm or immunosuppressive therapy and no family history of malignant tumors. On physical examination, lymphoadenopathy was absent. The lung and heart were normal. Liver was palpable 2 cm and spleen 2 cm below the costal margin. The hematological examination results were: white blood cell (WBC) count, 36.7×10^9/l, with 3% myelocytes, 8% metamyelocytes, 25% bands, 56% polymorphonuclear leukocytes, 1% eosinophils, and 7% lymphocytes (Fig. 1A); hemoglobin (Hb), 10.1 g/dl; platelet (Plt) count, 190×10^9/l; lactate dehydrogenase (LDH), 787 IU/l (normal 180–420 IU/l); erythrocyte sedimentation rate, 15 mm/hr; and leukocyte alkaline phosphatase (LAP) score, 351. The bone marrow showed grossly hypercellular with marked myeloid hyperplasia with 2.8% blasts. The myeloid:erythroid ratio was 8.6:1 (Fig. 1B). Cytogenetic analysis revealed 46,XX,20q- karyotype in all 20 analyzed bone marrow cells (Fig. 2). DNA hybridizations, using a 0.6 kb HindIII-BamHI bcr probe and a 1.2 kb HindIII-BgIII bcr probe, disclosed no bcr rearrangement band. A microbiological screen was negative and extensive radiologic investigations failed to identify concomittant carcinoma. She was ultimately diagnosed as having neutro-

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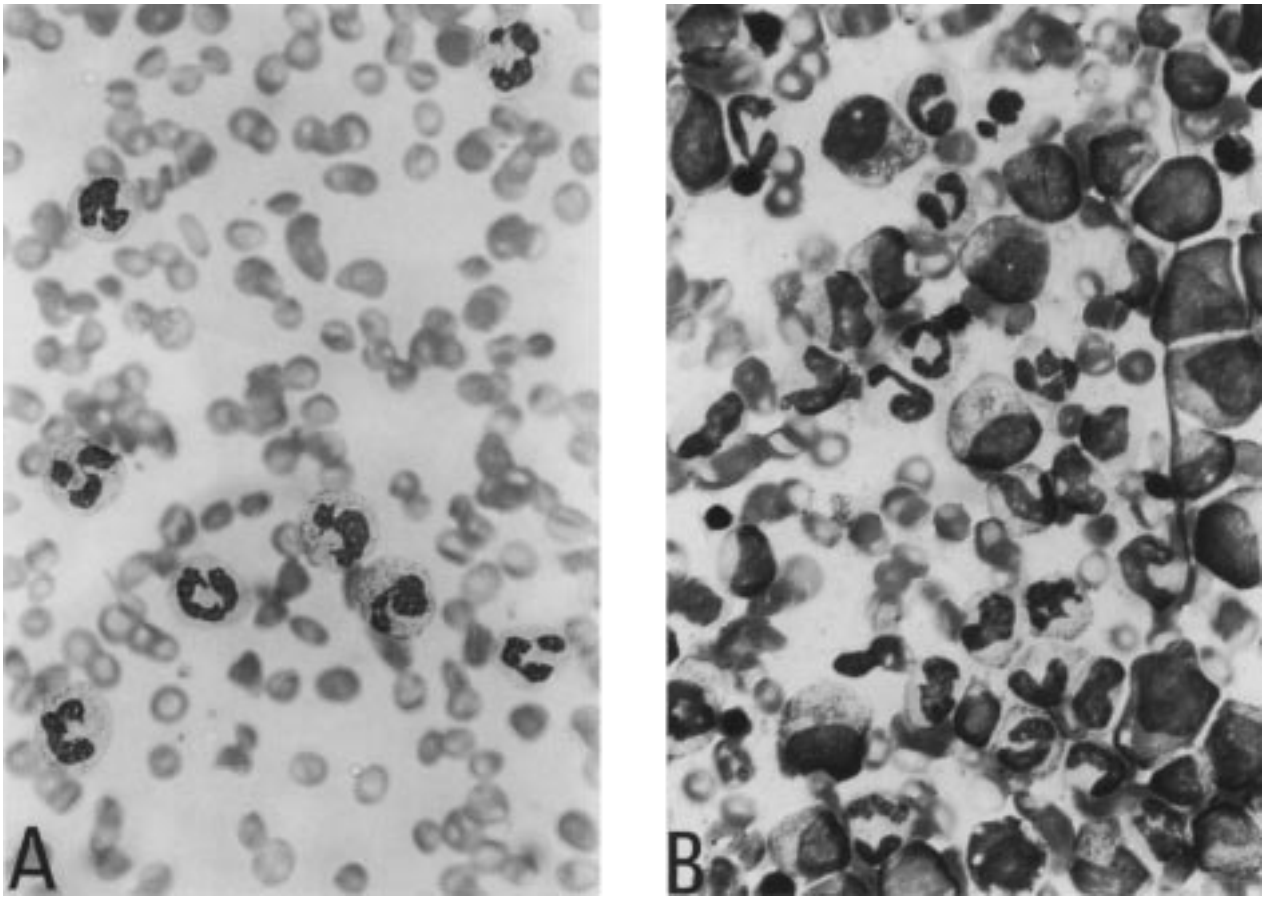

Fig. 1. A: Peripheral blood smear (May-Grunwald-Giemsa stain, original magnification, ×400). B: Bone marrow aspirate (May-Grunwald-Giemsa stain, original magnification, ×400). Mature neutrophilic granurocytosis was found.

philic leukemia. Although she was followed up without special treatment, the WBC count and the splenic size increased, and she had received carboquon from January 1988. Both the hematological and clinical findings had been stable for 7 years.

The proliferation of blasts was detected in July 1995. The hematological data were: WBC count, 26.5×10^9/l with 46% blasts; Hb, 8.7 g/dl; Plt count, 65×10^9/l. Cytogenetic analysis revealed 46,XX,20q- karyotype in all 20 analyzed cells. The blasts were positive for myeloperoxidase, CD13, CD33, and HLA-DR. The diagnosis of myeloid crisis was made. Although she was treated with interferon-α, it had no effect, and she died in July 1995. No autopsy was performed.

DISCUSSION

You and Weisbrot [1] have proposed the criteria for the diagnosis of CNL. In addition to this criteria, the absence of Ph chromosome [2,3] and bcr-abl hybrid gene [4,5] are also important findings for the dignosis of CNL. The profiles of our patients corresponded to these findings, and she was diagnosed as having CNL. Our patient lacked eosinophilia, basophilia, and thrombocytosis, all of which are usually seen in patients with standard CML. Some investigators have also pointed out the same findings [2,6]. Absence of these findings is helpful in distinguishing CNL from CML.

In our patient, the clonal nature of CNL is proved by the karyotypic aberrations. However, it is difficult to show the clonality of myeloid proliferation in patients with CNL who lacked cytogentic abnormalities. DNA hybridization is a useful method which analyses the clonality of the myeloid proliferation [5,7]. It is of note that one case with CNL and myeloma showed polyclonal myeloid proliferation with DNA hybridization [7]. Therefore, the clonal nature of myeloid proliferation should be proved for the diagnosis of CNL.

Most well-documented cases with CNL showed normal karyotype [1,4,5]. To our knowledge, four cases with

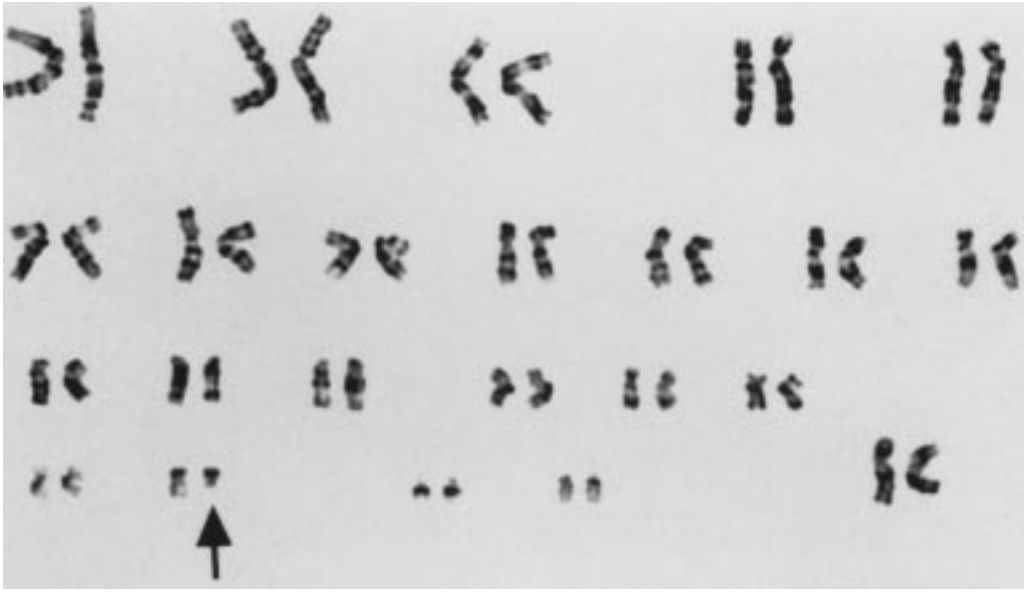

Fig. 2. G-banding bone marrow metaphase and its karyotype showing deletion of the long arm of chromosome 20 (arrow).

TABLE I. Patients With CNL Who Showed Cytogenetic Abnormalities

No.	Age	Sex	Chromosomal aberrations	References
Untreated patients				
1	65	F	46, XY, t(1;20)(q213q131)	[8]
2	71	M	47, XY, +8	[6]
3	67	F	46, XX, 20q−	Present case
Previously treated patients				
4	73	M	46, XX, +9,20q−	[3]
5	74	M	46, XY, del(20)(q11)	[9]

CNL who show clonal cytogenetic abnormalities have been reported [3,6,8,9]. In addition to our patients, we reviewed these cases (Table I). One case showed concomittant monoclonal gammopathy (no. 1), and CNL is associated with polycythemia vera (PV) in one case (no. 5). Three cases show cytogenetic abnormalities before treatments were started, whereas two cases received chemotherapy and/or radiation before the cytogenetic abnormalities were detected. In the latter group, the cytogenetic abnormalities may reflect the clonality of their CNL, however, it is also possible that the abnormalities are dependent on the influence of treatment. Four of five patients have the abnormality of long arm of chromosome 20 (nos. 1, 3, 4, and 5), and three of them showed deletion of long arm of chromosome 20 (nos. 3, 4, and 5), so that this abnormality is the most frequent cytogenetic change in patients with CNL. Indeed, this cytogenetic abnormality is not specific to CNL, since this is also found in patients with other hematological disorders, including myeloproliferative disorders, myelodysplastic syndromes, and acute leukemia [10]. The molecular analyses of 20q deletions in patients with myeloproliferative disorders and myelodysplastic syndromes have been reported, and some candidate tumor suppressor genes locate on commonly deleted regions of chromosome 20 [11,12]. These findings suggest that candidate tumor suppressor gene, that is associated with the development of CNL, is also located on the long arm of chromosome 20.

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